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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BAUGHMAN, MOLLY E	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
05/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,249	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/12/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments, in the reply filed 3/12/2007, with respect to claim rejection(s) of under 35 U.S.C. 102(b), and claim rejections under 35 U.S.C. 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made under 35 U.S.C. 102(e) in view of Nova et al. (US 6,340,588), and double patenting in view of Chee et al. (US 7,060,431).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 29-30, 33-34, 38-39, 40-45, 48-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Nova et al. (US 6,340,588 A1).

Regarding claims 29-30, 34, 38, 40, and 52, Nova teaches combinations, called matrices with memories, of matrix materials that are encoded with an optically readable code. The matrix materials are those that are used as solid supports in solid phase chemical and biochemical syntheses. The memories include electronic and optical

storage media and also include optical memories. Molecules and biological particles that are in proximity or in physical contact with the matrix combination can be labeled by programming the memory with identifying information (abstract). Molecules such as antigens, antibodies, ligands, proteins, and nucleic acids, and biological particles, such as phage and viral particles and cells that are associated with, such as in proximity or in physical contact with the matrix combination or linked via information stored in a remote computer, can be electromagnetically tagged by programming the memory with data corresponding to identifying information or can be tagged by imprinting or encoding the matrix with identifying information (col.6, lines 23-33). Nova states the combinations are particularly advantageous for use in multianalyte analyses, assays in which an electromagnetic signal is generated by the reactants or products in the assay (col.7, lines 20-31). This also includes multianalyte analysis wherein many analytes in a single specimen are measured (col.28, lines 65-67).

Regarding claims 29, 48-51, the matrix materials are any materials that are routinely used in chemical and biochemical assays and may be in the form of particles or may be continuous in design, such as a test tube or microplate, 96 well, 384 well, 1536 well, or higher capacity formats or other such microplates and microtiter plates (col.7, lines 40-53; col.25, lines 23-28). If the matrix is continuous, the data storage device [memory] may be placed in, on or under the matrix medium or may be embedded in the material of the matrix or or removably attached, such as in a sleeve designed to fit on the matrix (col.8, lines 14-18). In embodiments where plates include a bar code, the bar code may also be used in combination with modules that are fitted into

the frames of 96 wells, or higher density formats. Separate containers or strips of containers are designed to fit into microplate frames. Each such container may be encoded with a bar code so that, upon removal from the strip, the container, thereby, its contents or history, may be identified (col.8, lines 19-34). In some instances, the container, such as the microtiter plate is the matrix material, where it can be used to contact the molecule or biological particle with the matrix material. The recording device is placed in or on the matrix or is embedded, encased or dipped in the matrix material (col.10, lines 31-46). In preferred embodiments, the matrix with memory with linked molecules are mixed and reacted with a sample according to a screening assay protocol and those that react are isolated (col.14, lines 63-67). In one example, Nova describes an assay where the matrices with memories are activated to bind immunoglobulins and with on-board information specifying their relative locations in the array are dipped into the wells of microplates containing hybridoma cells. After incubation, they are withdrawn, rinsed, removed, and exposed to labeled antigen (col.106, lines 62-67 and col.107, lines 1-23).

Regarding claims 33-34, Nova discusses various multiplex assays where optically coded or electronically tagged libraries of oligonucleotides, peptides, proteins, non-peptide organic molecules, phage display, viruses and cells are used where the combinations are particulate matrices, such as polystyrene beads, with attached memories, and continuous matrices, such as microtiter plates, with a plurality of embedded or attached memories. These combinations can be use in any application in which support-bound molecules are used. Some examples include labeling DNA and

RNA, in nucleic acid amplification reactions, nucleic acid synthesis, nucleic acid sequencing, high throughput screening, hybridization reactions, receptor binding assays, isolation and purification of target macromolecules, etc. (col.15, lines 10-23, 29; col.76, lines 13-52; col.80, lines 3-10; col.82, lines 27-37).

Regarding claim 39, Nova also discusses embodiments where a plurality of particles, such as a polystyrene bead, are sealed in chemically inert porous supports, such as polypropylene formed so that it has pores of a selected size that excludes the particles but permits passage of the external medium. The support may be just porous or a semi-permeable inert material (col.10, lines 52-67 – col.15, lines 1-7; col.34, lines 28-31). The particles usually have a 5-10mm range or smaller and size of 100 mm3 or less (col.24, lines 11-23; col.25, lines 3-6)

Regarding claims 41-44, Nova discusses assays where the targets are fluorescently labeled (col.16, lines 49-55; col.24, lines 56-67; col.29, lines4-12; col.103, lines 1-7; col. 93-96). Radioactive and non-radioactive energy transfer proximity assays, such as HTRF, and FRET assays, can also be used where a change in signal is generated when one fluorophore is excited when in close proximity to a second fluorophore (col.24, lines 56-67; col.78, lines 17-48; col.84, lines 11-26).

Regarding claim 45, Nova discusses in specific embodiments multianalytes immunoassays wherein analytes of interest are detected and quantitated simultaneously (col.96).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 31-32, 35-37, and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nova et al. (US 6,340,588 A1), as applied to claims 29-30, 33-34, 38-39, 41-45, 48-52 above, and further in view of Fodor et al. (U.S. 5,800,922).

The teachings of Nova are discussed above. Although Nova discusses a a substrate comprising a plurality of array locations, each array comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and further discusses using beads (i.e. microspheres) which inherently comprise a plurality of discrete sites, he does not specifically discuss the amount of bioactive agents such

array locations comprise; specifically, comprising from 10,000,000 to 2,000,000,000 bioactive agents per square centimeter (claim 35), 100,000 to 10,000,000 bioactive agents per square centimeter (claim 36), or 10,000 to 100,000 bioactive agents per square centimeter (claim 37). Although Nova discusses using the matrices with memories for nucleic acid amplification reactions, he does not specifically discuss the nucleic acids comprising single nucleotide polymorphisms (claims 31-32). While he discusses the method further comprising quantitating differences in concentrations of the target analytes, he does not specifically discuss the embodiment wherein the target analytes are mRNA (claim 46), or wherein the mRNA is quantitated in the presence of total cellular mRNA (claim 47).

Regarding claims 31-32, Fodor et al. disclose a method of producing a substrate having a plurality of positionally distinguishable sequence specific reagents, wherein the reagents could be polynucleotides, polymers, carbohydrates, polypeptides, etc. (page 2, lines 34-67, and page 6-7, lines 63-67; 1-5). The methods can also be coupled to a polymerase chain reaction (page 27, lines 17-19, and page 58, lines 23-26), wherein specific reagents (probes) can be used to detect one or more mismatched bases in a fluorescently labeled target (page 69, lines 17-67, page 4, lines 45-64).

Regarding claims 35-37, Fodor et al. disclose a method of generating the desired repertoire of oligonucleotide probes on a substrate, wherein the densities could range from 5 regions/cm^2 to an excess of one million regions/ cm^2 (page 20, lines 13-37).

Regarding claims 45-47, Fodor et al. disclose characterizing various samples by testing their mRNA sequence intent (page 29, lines 33-36, and 42-46). Furthermore,

they discuss defining the pattern of expression of mRNA, in comparison to other types of RNA, wherein different levels of RNA may be found in correlation to the developmental stage of the cell (page 30, lines 10-20).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the dipping apparatus of Nova et al. to apply the varying densities of bioactive agents at array locations as in claims 35-36 not only because Nova teaches using arrays comprising beads which inherently are capable of such densities of bioactive agents, Fodor et al. demonstrates the benefits of using such arrays which comprise different bioactive agents at such densities for faster and more efficient reactions. It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to further modify the method of Nova et al. to use the dipping apparatus for the detection of amplified nucleic acids comprising single nucleotide polymorphisms or to quantitate the differences in levels of specific mRNA in the presence of total cellular mRNA because Fodor et al. demonstrates that it was conventional in the art to use such multiplexing arrays for the detection of amplified nucleic acids comprising single nucleotide polymorphisms as well as for the simultaneous quantification of specific types of RNA molecules present in a sample. Therefore, the skilled artisan would have had a reasonable expectation of success in modifying the dipping apparatus of Nova et al. to include such densities of bioactive agents at said array locations and further use it for the detection of SNPs in amplifed nucleic acids, as well as for the quantification of specific mRNA in the presence of total cellular mRNA to the method of Landegren. It would have been *prima facie* obvious to

one of ordinary skill in the art at the time of the invention to carry out the claimed methods, use the claimed densities of bioactive agents as said array locations, detect amplified nucleic acids comprising SNPs, and detect specific mRNAs therein.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 29-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, and 9 of U.S. Patent No. 6,858,394. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and instant claims are drawn to a genus:species relationship.

8. Claims 29-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-24, and 31-58 of U.S. Patent No. 7,060,431. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and instant claims are drawn to a genus:species relationship. Specifically, said patent claims uses claim language of "contacting," where the specification includes embodiments where contacting includes dipping (see specification, col.18).

Summary

9. No claims are free of the prior art.

Conclusions

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 5/25/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

5/29/07